An Eye to the Future:

Training the Next Generation of Researchers

The CTSA consortium provides access to critical training opportunities for junior investigators. **BY LAURA BONETTA**

In New York City, a physician treating patients infected with the hepatitis C virus learns to conduct laboratory research to gain clues about how the virus sabotages the function of blood cells.

In St. Louis, a graduate student developing computer-based tests to study how the brain controls movement begins to collaborate with nurses and physicians to translate her research to patients with Parkinson's disease.

Meanwhile, in Portland, Ore., a physician committed to serving underserved populations receives education and training for conducting community-based research so that she can better address the health care needs of her patients.

CLINICAL AND TRANSLATIONAL SCIENCE AWARD CONSORTIUM

Creating a unique network of medical research institutions across the nation, the Clinical and Translational Science Award (CTSA) consortium is working to reduce the time it takes for laboratory discoveries to become treatments for patients. The consortium also is fulfilling the critical need to train the next generation of clinical and translational researchers through innovative advanced degree programs, mentoring, diverse collaborations and interdisciplinary teams. It brings together basic, translational and clinical investigators; community clinicians; clinical practices; networks; professional societies; and industry to develop new professional interactions, programs and research projects. Currently consisting of 38 research institutions, by 2012, when the program is fully implemented, the consortium will connect approximately 60 CTSA sites. The consortium is led by NCRR.

These three researchers represent the future of translational research — the translation of scientific and technical advances into tangible benefits for patients and communities. Each individual has benefited from the training and education provided through innovative programs at medical institutions across the nation with support from NCRR's Clinical and Translational Science Award (CTSA) program. Although the institutions' training programs have diverse strengths and goals, they share the common mission of providing junior investigators with the knowledge, skills and resources they need to conduct science that will improve human health.

"The things that bind all the CTSA institutions together are commitments to train the next generation of translational researchers, to share best practices and to work collaboratively," said Frederick J. Meyers of the University of California, Davis, chair of the Research Education and Career Development Key Function Committee for the CTSA consortium. "We expect to develop a fundamentally different group of researchers. They are still well-grounded in the discipline of science, but they also are knowledgeable of regulatory and ethical requirements, able to engage in team science and passionate about bringing discoveries to patients."

The training programs developed at each CTSA site span the entire spectrum of research, from basic to preclinical to clinical studies, providing future translational scientists with "core competencies," consisting of the necessary knowledge, attitudes and skills required to conduct interdisciplinary research. These

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competencies are taught primarily through didactic courses that lead to master's degrees in clinical research and, in some cases, doctoral degrees in translational and clinical research, tailored to an individual's career aspirations. In addition, these programs provide opportunities to expose future physician-scientists to interdisciplinary team science. Another important component of the training programs is the quality mentoring that participants receive from established scientists, who serve as guides and role models for the careers the junior investigators want to pursue.

Although many of these programs are still in their infancy — the CTSA program was just launched in 2006 — their effects can be seen clearly in the stories of individuals who have participated in them.

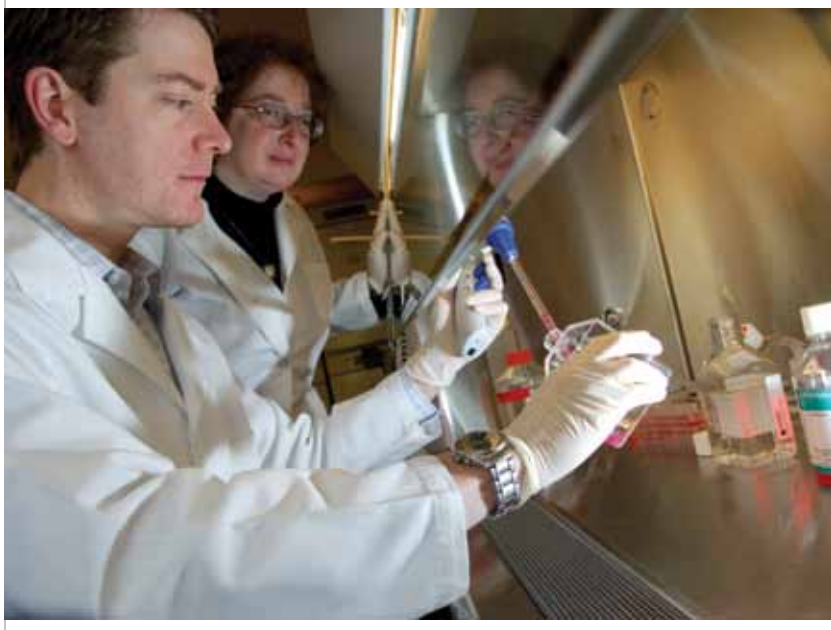
BASIC DISCOVERY TO TRANSLATIONAL RESEARCH

Edgar Charles treated patients infected with the hepatitis C virus during his residency in internal medicine and fellowship in infectious diseases at New York University School of Medicine. This viral infection is one of the most common causes of chronic liver disease and organ transplantation in the United States. One of the many puzzling aspects of the disease is that some patients also develop an inflammation of the blood vessels, probably due to the presence in the blood of certain types of immunoglobulin. These molecules are normally produced by the plasma cells of the immune system to identify and neutralize foreign substances, such as bacteria and viruses, and in some diseases, they also can attack normal cells and tissues in the body. Additionally, some patients with hepatitis C infection suffer from a type of immune system cancer called non-Hodgkin's lymphoma.

Charles reasoned that more research was needed to fully understand the disease and, in particular, the role B cells of the immune system were playing in it. Although the two-year fellowship he had undertaken at New York University included a year of research, Charles said that "to do more research seriously, I would have to have more training." He was not, however, sure of how to go about getting that training.

After considering different training programs, he learned about the Clinical Scholars Program offered by The Rockefeller University's Center for Clinical and Translational Science — a member of the CTSA consortium. This three-year program, which leads to a master's degree in clinical and translational research, gives a junior investigator, typically a physician, the opportunity to join the laboratories of established scientists who provide mentorship for the scholar's research. The mentored research project is complemented by a curriculum that provides education in several core competencies, including the responsible conduct of research, biostatistics and standards for conducting clinical studies. "Once I looked into the program, it was a very clear choice for me to do it," Charles said.

In his early efforts, he arranged to conduct a research project to study B-cell function in patients with hepatitis C infection under the joint supervision of Charles Rice, a renowned virologist, and Lynn Dustin, a distinguished immunologist, at The Rockefeller University. Charles first had to



■ Edgar Charles performs experiments on blood cells from patients infected with the hepatitis C virus as mentor Lynn Dustin, an immunologist at The Rockefeller University in New York City, looks on. Charles undertook the research as part of the Clinical Scholars Program offered by Rockefeller's Center for Clinical and Translational Science, a member of the CTSA consortium. A recent graduate of the program, Charles has now received a coveted NIH Mentored Clinical Scientist Development Award to launch his career as a physician-scientist.

PHOTO BY ZACH VEILLEUX, THE ROCKEFELLER UNIVERSITY

■ Jennifer Semrau, a graduate student at the CTSA-supported Brain, Behavior and Performance Unit (BBPU) at the Washington University in St. Louis Institute of Clinical and Translational Sciences, monitors a Parkinson's disease patient's hand movements as he responds to visual cues on a computer screen. Semrau, who is conducting her doctoral research in a bioengineering laboratory, benefited from training and resources provided by the BBPU, which allowed her to apply her research to patients.

obtain blood samples from patients. For this aspect of the study, the assistance he received from the Center for Clinical and Translational Science was invaluable. The Center's staff helped Charles obtain approval for his proposal from his institutional review board (IRB) — typically a daunting undertaking — such that he was able to quickly start his research. (An institution's IRB considers ethical, policy and regulatory issues regarding patient research.) Nurses and other medical staff then helped Charles recruit suitable patients and collect samples.

In Dustin's laboratory, Charles began learning how to operate as a scientist. "Edgar was beautifully trained clinically, and he had done some bench work before, but when he first came to my lab, he was not yet able to function independently as a scientist," Dustin said. "I started out suggesting experiments for him and teaching him procedures. I also critiqued his writing for grant applications and papers." In the laboratory, Charles learned to carry out different sophisticated molecular and biochemical analyses on the B cells he isolated from patients' blood.

Through his research, Charles discovered that the hepatitis C virus causes certain B cells that produce a particular type of immunoglobulin to greatly increase in numbers. He published his findings in the prestigious scientific journal *Blood* in February 2008. Based on this work and a grant proposal he wrote describing future studies, Charles received a Mentored Clinical Scientist Development Award from NIH's National Institute of Allergy and Infectious Diseases. The award provides support for up to five years to help recipients transition from mentored research to an independent research position. "Developing the skills to become an independent clinical investigator is precisely the goal we set for trainees in our master's program, and so we are delighted with Dr. Charles' success," said Barry Coller, director of the Center for Clinical and Translational Science.

Charles started with a medical problem and used basic laboratory science to find possible answers for it. His findings are providing insights into what causes the disease symptoms associated with hepatitis C infection and may someday offer clues on developing treatments to alleviate such symptoms. The next step in the continuum of translational and clinical research is the translation of laboratory findings to patients — a step that requires its own set of competencies, as well as a dedicated infrastructure for clinical studies.

ADVANCING RESEARCH FROM LAB TO PATIENT

The infrastructure needed for clinical studies exists in places like the Brain, Behavior and Performance Unit (BBPU) at the Washington University in St. Louis Institute of Clinical and Translational Sciences — a CTSA consortium member. "The BBPU really permits junior investigators to do patient-oriented research," said unit director Joel S. Perlmutter. "We provide support for getting the initial findings, so that they can use those results to apply to traditional sources of funding." Without this kind of support, applying basic scientific findings to human studies would be a much more challenging proposition. "The BBPU makes this kind of effort move forward in a much more efficient manner," Perlmutter explained. "It really enhances the chances of bringing research findings to patients."

The BBPU provides collaboration, consultation and training for clinical research studies of the nervous system. Kurt Thoroughman is one of many basic researchers taking advantage of these resources. A biomedical engineer interested in how the brain's complex wiring controls movement, Thoroughman has designed several experimental setups that give visual feedback to people as they perform certain movements. Such feedback tells them, for example, if they are moving a hand in the correct direction — if not, people automatically adapt the arm movement according to the feedback. "Over the years, we have come up with very precise tasks and tests of human performance," he explained. "Previously, it was thought that what you learn can change but *how* you learn it is fixed. But we discovered that both what and how you learn can change very quickly."

With graduate student Jennifer Semrau, Thoroughman decided to try the tests they had developed on Parkinson's

PHOTO BY SCOTT FERGUSON, FK PHOTO

disease patients. In particular, Semrau was interested in finding out whether the disease affects the brain's ability to adapt to a changing environment. With advice from staff at the BBPU, Semrau designed a protocol in which Parkinson's patients train on a computer to move a stylus from one point to another. After a while, the computer begins "tricking" them by giving them odd visual cues — for example, indicating that they are moving the stylus at an angle when in fact they are moving it in a horizontal line. The patients then adapt their movements to such cues.

A research coordinator helped Semrau obtain IRB approval, and a patient coordinator recruited suitable subjects with the aid of an extensive patient database. The BBPU has been instrumental in countless similar studies, providing training and assistance to scientists who would otherwise have little opportunity to work with patients. In parallel, the Institute of Clinical and Translational Sciences provides a number of didactic courses for translational researchers, including a master's degree in clinical investigation. "We don't try to reproduce those courses at the BBPU," Perlmutter said. "Instead we provide hands-on experience, as well as assistance with IRB applications, regulatory procedures and how to design a study protocol. We are really marrying the didactic with the practical."

Semrau had a unique opportunity to take findings developed in a basic research laboratory to Parkinson's patients. But once basic findings are translated to patient research, there is one more step in the continuum of translational and clinical science. If that research is to benefit human health, it has to reach out to communities.

MOVING INTO PRACTICAL FIELD EXPERIENCE

The many roles of a translational researcher include bringing innovations into communities as well as determining the health needs of people in the community and how best to address them. This step, however, requires a set of skills that are not often taught in traditional courses. "In medical school, the focus is on the patient, on the one-to-one encounter between the patient and physician," said Cynthia Morris, director of education and career development at the Oregon Clinical and Translational Research Institute of Oregon Health & Science University — another CTSA consortium member.

The Master of Clinical Research program was designed to provide instruction to a broad spectrum of researchers — from graduate and medical students to full professors and practicing physicians. "Everyone has a different take on what they are learning based on their background and experience," Morris said. "That means that they all can learn from one another. They get used to the idea of working together in teams."

The unique aspect of the program is that half of it focuses on teaching core competencies, whereas the other half allows students to pick and choose from a variety of courses based on their interests and career goals. Many of these "electives" have a strong focus on community-based research. "At least half of the students who go through our program are here because they want to learn how to do community-based research," Morris said. "In other words, how to translate findings of lab research into practice and then into populations."

CORE COMPETENCIES FOR CLINICAL AND TRANSLATIONAL INVESTIGATOR TRAINING

The task of CTSA education programs is to prepare the next generation of investigators to conduct clinical and translational research that will address the health care challenges faced in the United States. Creating a recognizable discipline centered on clinical and translational science will help build this workforce. To help establish the discipline, NCRR and the CTSA Education and Career Development Key Function Committee have drafted national standards for core competencies in clinical and translational science. The thematic competencies identify common, basic elements that should shape the training experiences of junior investigators by defining skills, attitudes and behaviors that can be shared across multidisciplinary teams of clinician-scientists. The overall goal is to create a competency-based education for training clinician-scientists that will define the discipline of clinical and translational science. Below are the training competencies for master's and doctoral candidates:

- Identify major clinical/public health problems and relevant research questions
- Critique the literature regarding the status of a health problem
- Design a study protocol for clinical and translational research
- Study methods, design and implementation
- Laboratory, clinical and population research methods
- Statistical methods and analysis
- Bioinformatics
- Conduct of responsible research
- Scientific communication skills and dissemination
- Population diversity and cultural competency
- Principles of community engagement in clinical and translational research
- Translational teamwork
- Leadership and professionalism
- Cross-disciplinary training and mentoring
- Advancement of knowledge

That was certainly the case for Rachel Solotaroff. After completing her medical degree and residency, she wanted to do research with underserved populations. "But I did not know how to go about it," she recalled. She initially enrolled in a master's program and took several courses in fundamental epidemiology and statistics — skills she was lacking. She also participated in an interactive course that taught her how to prepare a grant application. "That course was really fundamental," Solotaroff said. "I did not know how to formulate a research question. I was not trained to think like a researcher. It is not something that came naturally to me. But that course really taught me how to do it."

As a result, she was able to write a successful application to a fellowship that allowed her to study how patients with chronic diseases, such as diabetes, cope with self-managing their own health care with sporadic or no health insurance coverage. After spending two years on this research project, she became the medical director at Central City Concern, a social-service agency based in downtown Portland that provides medical, housing and employment assistance to a predominantly homeless population, including many individuals addicted to drugs.

A SMORGASBORD OF COURSES

Thomas Pearson, co-principal investigator for the CTSA at the University of Rochester Medical Center in New York, is creating a database of courses that will be available to all students and researchers at any institution at the click of a button. "The CTSA consortium has done a nice job to create a core curriculum in clinical and translational research," Pearson said. But not every institution is able to provide high-level courses in specialized fields, such as proteomics or genomics. Such courses are not core competencies but are, as Pearson put it, "icing on the cake."

As a result, he has been collecting high-quality courses on important but more specialized topics developed at each CTSA institution. Once collected and reviewed by a panel of advisors, the courses will be posted on the Web as online lectures, Webinars, slide presentations and other Internet-friendly formats. "We are making a CTSA national consortium," Pearson said "This is just one way to become stronger than our parts."

In addition to making hundreds of courses available online, the Rochester CTSA has a pilot program to allow visiting professors to teach courses at different institutions as a "traveling show." Also, the program will provide scholarships for students to attend courses offered at different sites. "The idea is to give people at CTSA institutions more opportunities," Pearson said. "If I have a medical student interested in proteomics, I can tap the best teachers anywhere."

■ Cynthia Morris (seen here on the right) directs the Clinical Research Education program at the Oregon Clinical and Translational Research Institute (OCTRI) of Oregon Health & Science University (OHSU). In this photo, Morris is working with Melanie Gillingham, an early-career investigator who completed the Clinical Research Education program as a postdoctoral fellow at OHSU. Gillingham now has an OCTRI pilot grant and is also funded by the National Institute of Diabetes and Digestive and Kidney Diseases. She mentors medical students on their first research projects.

In her new position, Solotaroff is constantly confronted with a slew of questions related to the relationship between homelessness, addiction and health that she would like to systematically study. "Some of the questions I have come from things I see every day: 'How do you manage chronic pain in people with addiction?' Or 'How do you cope with the rapid weight gain and obesity in early withdrawal?'" She is confident she will be able to embark on such studies because of the training she received during her master's program. "I also made many contacts with researchers at Oregon Health & Science University," Solotaroff said. "I will be contacting some of those researchers to establish collaborations."

THE FULL RANGE OF TRAINING

Advances in biomedical research, computer science and informatics, and imaging and other technologies are providing unprecedented opportunities to improve human health. Yet transforming those advances into practical benefits for patients and communities requires a broad range of knowledge and skills specific to translational research. Such knowledge and skills are best acquired through carefully planned and innovative programs that incorporate didactic courses; hands-on experiences; mentorship; and participation in large, interdisciplinary teams. The training programs designed by CTSA institutions incorporate these components and give the new investigators sufficient flexibility to embark on individualized career pathways. ■

PHOTO COURTESY OF KENT ANDERSON